ACUTE TOXICITY SUMMARY

ISOPROPYL ALCOHOL

(isopropanol, 2-propanol, dimethylcarbinol, propyl alcohol)

CAS Registry Number: 67-63-0

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level 3,200 µg/m³

Critical effect(s) irritation of the eyes, nose and throat.

Hazard Index target(s) Eyes; Respiratory System

II. Physical and Chemical Properties (HSDB, 1993 except as noted)

Description colorless liquid

Molecular formula C₃H₈O Molecular weight 60.09

 Density
 0.78505 g/cm³ @ 20°C

 Boiling point
 82.5°C @ 760 mm Hg

Melting point -88.5°C

Vapor pressure $44.0 \text{ mm Hg} \otimes 25^{\circ}\text{C}$ Flashpoint 11.7°C (closed cup)Explosive limitsupper = 12.0%

lower = 2.0%

Solubility soluble in benzene, miscible with most organic solvents,

slightly soluble in water, alcohol, and acetone

Odor threshold 19 ppm (geometric mean) (AIHA, 1989)

Odor description sharp (AIHA, 1989)

Metabolites acetone

Conversion factor 1 ppm = $2.45 \text{ mg/m}^3 \otimes 25^{\circ}\text{C}$

III. Major Uses or Sources

Isopropyl alcohol has wide use in consumer products such as mild skin disinfectants and astringents. It is also used as a solvent for cellulose nitrate.

IV. Acute Toxicity to Humans

Symptoms of acute poisoning include dizziness, incoordination, headache, and confusion. Vomiting, hematemesis, diarrhea, and hypotension may occur following ingestion of large quantities of isopropyl alcohol. Late manifestations include aspiration pneumonia and kidney and liver dysfunction (Reprotext, 1993). The oral LOAEL for isopropyl alcohol is reported as 233 mg/kg (RTECS, 1993).

Irritation of the mucous membranes of the upper respiratory tract may occur following inhalation of isopropyl alcohol. Ten human subjects were exposed for 3-5 minutes to 400 or 800 ppm (1,000 or 2,000 mg/m³) isopropyl alcohol (Nelson *et al.*, 1943). Exposure to 400 ppm isopropyl alcohol produced mild irritation of the eyes, nose, and throat. When exposed to 800 ppm the majority of the subjects declared the atmosphere unsuitable for a prolonged exposure. The subjects indicated, however, that prolonged exposure to 200 ppm would not be objectionable.

Predisposing Conditions for Isopropyl Alcohol Toxicity

Medical: Persons with eye, skin, respiratory or neurological conditions and diabetics may be

more sensitive to the toxic effects of isopropyl alcohol (Reprotext, 1999).

Chemical: Individuals exposed to acetone, carbon tetrachloride, or n-hexane may be at

increased risk for adverse effects when exposed simultaneously to isopropyl

alcohol (Reprotext, 1999).

V. Acute Toxicity to Laboratory Animals

A 4-hour rat LC_{Lo} of 16,000 ppm (39,000 mg/m³) isopropyl alcohol is reported (Carpenter *et al.*, 1949). Reduced ciliary activity and epithelial damage in the nasal mucosa of guinea pigs were observed following a 24-hour exposure to 400 ppm (1,000 mg/m³) isopropanol. Complete recovery from the exposure occurred within 2 weeks. Exposure at 5,500 ppm (13,000 mg/m³) resulted in similar damage requiring more than two weeks for complete recovery (Ohashi *et al.*, 1988). A 10-minute RD₅₀ of 17,693 ppm (43,000 mg/m³) for mice has been reported (Kane at al., 1980).

VI. Reproductive or Developmental Toxicity

No human reproductive studies and only a limited number of animal studies on the effects of isopropyl alcohol were available. Pregnant rats exposed to 3,500, 7,000, and 10,000 ppm (8,600, 17,000, and 25,000 mg/m³) isopropanol for 7 hours per day on days 1-19 of gestation exhibited signs of maternal toxicity, indicated by retarded weight gain, following exposure to 7,000 ppm or greater. Signs of narcosis were observed in the dams exposed to 10,000 ppm. Fetal weight was reduced in all three exposed groups in a dose-dependent manner; increased skeletal and visceral malformations were observed following exposure to 7,000 ppm (Nelson *et al.*, 1988).

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects) 1.3 ppm (3,200 µg/m³)

Study Nelson et al., 1943
Study population ten human subjects
Exposure method 400 ppm for 3-5 minutes

Critical effects mild irritation of the eyes, nose and throat

LOAEL 400 ppm

NOAEL 200 ppm (implied)

Exposure duration 4 minutes

Extrapolated 1 hour concentration 13 ppm (200 1 ppm * 0.067 h = C 1 * 1 h)

(see Table 12 for information on "n")

LOAEL uncertainty factor1Interspecies uncertainty factor1Intraspecies uncertainty factor10Cumulative uncertainty factor10

Reference Exposure Level 1.3 ppm (3.2 mg/m³; 3,200 μg/m³)

Ten human subjects, exposed for 3-5 minutes to 400 ppm (1,000 mg/m³) isopropyl alcohol, reported mild irritation of the eyes, nose and throat. The study indicates a 4 minute LOAEL of 400 ppm. The subjects indicated that exposure to 200 ppm would be tolerable, which implies a NOAEL of 200 ppm. This 4 minute NOAEL was time adjusted to 1 hour. An uncertainty factor of 10 was applied to the 200 ppm NOAEL to account for the susceptibility of sensitive individuals.

Level Protective Against Severe Adverse Effects

Rats were exposed for 6 hours to 0, 500, 1,500, 5,000, or 10,000 ppm isopropyl alcohol (Gill *et al.*, 1995). Signs of narcosis and concentration-related decreases in motor activity were observed in rats exposed to 5,000 or 10,000 ppm. Slight but statistically significant decreases in motor activity were observed in male, but not female, rats exposed to 1,500 ppm isopropyl alcohol. No adverse effects were observed in rats exposed to 500 ppm isopropyl alcohol. Narcosis during isopropanol exposure at 1,500 and 5,000 ppm was also noted in a chronic inhalation study by Burleigh-Flayer *et al.* (1994). A 6-hour NOAEL of 500 ppm is defined from this study. An uncertainty factor of 10 was applied to account for interspecies differences. An additional uncertainty factor of 10 was applied to account for sensitive individuals. An equivalent 1-hour exposure concentration was estimated from the reported 6-hour NOAEL using the equation $C^n * T = K$, where n = 2. The resulting level protective against severe adverse effects is 12 ppm (29 mg/m³).

A TLV-TWA of 400 ppm is reported by ACGIH (1991) based on findings by Nelson *et al*. (1943); the NRC-EEGL of 400 ppm is based on the TLV (NRC, 1984). However, the reported 3-5-minute exposure to 400 ppm was not extrapolated to a 1-hour equivalent by NRC. Using the

equation $C^n * T = K$, where n = 1, the equivalent 1-hour exposure is 20 ppm. This is consistent with our use of the animal studies. In addition, the recent data described above (Gill *et al.*, 1995) were not available to ACGIH or NRC when determining these values.

Level Protective Against Life-threatening Effects

No recommendation can be made due to the limitations of the database.

NIOSH (1995) lists an IDLH of 2,000 ppm (4,900 mg/m³). The IDLH is based strictly on safety considerations and is 10% of the lower explosive limit of 2%.

VIII. References

American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Cincinnati (OH): ACGIH; 1991. p. 828-830.

(AIHA) American Industrial Hygiene Association. Odor thresholds for chemicals with established occupational health standards. Akron (OH): AIHA; 1989. p. 21.

Burleigh-Flayer HD, Gill MW, Strother DE, Masten LW, McKee RH, Tyler TR, Gardiner TH. Isopropanol 13-week vapor inhalation study in rats and mice with neurotoxicity evaluation in rats. Fundam Appl Toxicol 1994; 23:421-428.

Carpenter CP, Smyth HF Jr, Pozzani UC. The assay of acute vapor toxicity, and the grading and interpretation of results on 96 chemical compounds. J Ind Hyg Toxicol 1949;31(6):343-346.

Gill MW, Burleigh-Flayer HD, Strother DE, Masten LW, McKee RH, Tyler TR, Gardiner TH. Isopropanol: Acute vapor inhalation neurotoxicity study in rats. J Appl Toxicol 1995;15(2):77-84.

(HSDB) Hazardous Substances Data Bank. National Library of Medicine, Bethesda (MD) (CD-ROM Version). Denver (CO): Micromedex, Inc.; 1993. (Edition expires 11/31/93).

Kane LE, Dombroske R, Alarie Y. Evaluation of sensory irritation from some common industrial solvents. Am Ind Hyg Assoc J 1980;41:451-455.

(NRC) National Research Council. Committee on Toxicology. Emergency and continuous exposure limits for selected airborne contaminants. Vol 2. Washington (DC): National Academy Press; 1984.

Nelson BK, Brightwell WS, MacKenzie-Taylor DR, Khan A, Burg JR, Weigel WW. Teratogenicity of n-propanol and isopropanol administered at high inhalation concentrations to rats. Food Chem Toxicol 1988;26(3):247-254.

Nelson KW, Ege JF Jr, Ross M, Woodman LE, Silverman L. Sensory response to certain industrial solvent vapors. J Ind Hyg Toxicol 1943;25(7):282-285.

(NIOSH) National Institute for Occupational Safety and Health. Chemical listing and documentation of revised IDLH values (as of March 1, 1995). Available at http://www.cdc.gov/niosh/intridl4.html.

Ohashi Y, Nakai Y, Koshimo H, Esaki Y, Ikeoka H, Horiguchi S, *et al.* Toxicity of isopropyl alcohol exposure in the nasal mucociliary system in the guinea pig. Environ Res 1988;46:25-38.

(RTECS) Registry of the Toxic Effects of Chemical Substances. National Institute for Occupational Safety and Health, Cincinnati (OH) (CD-ROM Version). Denver (CO): Micromedex, Inc.; 1993. (Edition expires 11/31/93).

Reprotext ® System. Dabney BJ, editor. Denver (CO): Micromedex, Inc.; 1999. (Edition expires 1/31/1999).

Smyth HF Jr. Improved communication--Hygienic standards for daily inhalation. Am Ind Hyg Assoc Q 1956;17(2):129-185.